REMARKS

Entry of the foregoing and favorable reconsideration and reexamination of the subject matter, as amended, pursuant to and consistent with 37 C.F.R. § 112 and in light of the remarks that follow are respectfully requested.

Claims 13, 17 and 19 have been cancelled. Claims 6, 11, 16, 18 and 20 have been amended with respect to transitional language that immediately precedes the recitation of "SEQ ID NO:1", and claim 13 has been amended to modify the transitional language and by deleting the recitation "fragment".

Claim 10 has been amended to further specify the variant of polynucleotides designated as SEQ ID NO:1 or 3, in terms of having one of two types of structural modifications relative to the parent sequence, namely a nucleotide substitution or a nucleotide deletion. The amendatory language is supported by the disclosures on page 11, first and second paragraphs.

Claim 20 has been amended to recite an intended use, namely "gene therapy".

Newly added claim 21 relates to a variant of polynucleotide designated as SEQ. ID NOS: 1 or 3, wherein a polypeptide encoded by said polynucleotide variant binds βTrCP or RasSF1 respectively, and wherein said polynucleotide variant has at least 95 % homology with SEQ. ID NO: 1 or 99.999% homology with SEQ. ID NO: 3. This amendatory language is supported by the disclosures on page 10, last paragraph.

Newly added claim 22 differs from claim 20 in that it does not contain the recitations "pharmaceutical" and "pharmaceutically acceptable", support for which is contained throughout the specification, *e.g.*, pages 17-21.

Applicants submit that no new matter has been added via these amendments. Accordingly, entry of the amendment is respectfully requested.

Claim 10 has been rejected under 35 U.S.C. § 112, first

paragraph, as lacking adequate written description for the full scope of variants encompassed by the claim. The Examiner purports that "naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material."

Claim 10 has been amended such that in addition to the binding specificity, it now recites that the variants of SEQ ID NO:1 or 3 possess one or two different types of structural modifications relative to the parent sequence.

Contrary to the allegations in the Action, the skilled artisan would easily be able to distinguish the claimed variants of SEQ ID NO:1 or 3 (presenting with one of the above modifications) encoding a polypeptide that bind βTrCP or RasSF1 from variants of SEQ ID NO:1 or 3 that do not possess that binding specificity and which are outside the scope of the claim, simply by using a prey/bait interaction protocol (two-hybrid screen) as illustrated in example 6 of the present specification. Indeed, a two-hybrid screen using either βTrCP or RasSF1, would enable the one skilled in the art to detect corresponding interacting polypeptide and then to determine whether such a variant encodes a polypeptide having the recited binding specificity.

The recitation of structural characteristics, along with the recitations of function of binding either βTrCP or RasSF1, renders the claims compliant with 35 U.S.C. § 112, first paragraph (written description). Thus, in view of the above, withdrawal of this rejection is respectfully requested.

Claims 13, 19 and 20 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. For the following reasons, this rejection is respectfully traversed as it pertains to claim 20. Since claims 13 and 19 have been cancelled, the rejection is now moot with respect to these claims.

The Examiner purports that the only utility asserted in the specification for a pharmaceutical composition comprising a genetically modified host cell is *ex vivo* gene therapy. Likewise, the specification does not contemplate a use for the pharmaceutical composition comprising a vector consisting as forth in claim 20 other than gene therapy.

Claim 20 has been amended and now relates to pharmaceutical composition *for use in gene therapy*. This claim is enabled by the specification. See paragraphs 155-163 and 169, and the prior art referenced therein.

Applicants traverse the rejection to the extent it would be applied to new claim 22. This claim is directed to a composition containing the vectors and a carrier. The specification teaches and enables several uses of the compositions, both pharmaceutical and non-pharmacecutical alike, including conducting bait-prey interactions, as expression systems for the polynucleotides, and in gene therapy. In such situations when multiple uses are disclosed, section 2164.01 (c) of the MPEP only requires applicants to enable one use. Therefore, withdrawal of the rejection is requested.

Claims 6, 9-11, 13 and 20 have been rejected under 35 U.S.C. § 102(b), as being anticipated by Cenciarelli et al. (1999)("*Cenciarelli*"). For the following reasons, this rejection is respectfully traversed with respect to claims 6, 9-11 and 20.

Cenciarelli teaches a nucleic acid sequence of 2151 base pairs (like AFi 29530). It does not teach a polynucleotide designated as SEQ ID NO:3 which has 1680 nucleotides. Neither does it teach a nucleic acid or polynucleotide consisting of SEQ ID NO:1, which contains 657 nucleotides, a vector comprising a polynucleotide consisting of SEQ ID NO:1, or a variant of SEQ ID NO:1 having a structural feature as recited in claim 10, as amended, (which do not include variants that encode longer polypeptides). Thus, claims directed to compositions and host

cells containing the polynucleotides are not anticipated by *Cenciarelli*.

New claim 21 is not anticipated by the cited reference. It is directed to a variant having at least 95 % homology with SEQ. ID NO:1 (RasSF1) is also different from *Cenciarelli* since a homology of 95% allows 32 nucleotide substitutions, deletions or additions (657 x 5/100), and may results in maximum to a nucleic acid of 689 base pairs in size. New claim 22 recites a polynucleotide "consisting of" SEQ ID NO:1; thus, it is not anticipated.

Withdrawal of this rejection is respectfully requested.

Claims 9 and 10 have been rejected under 35 U.S.C. § 102(b), as being anticipated by Entrez nucleotide sequence accession No AF061836. For the following reasons, this rejection is respectfully traversed.

The sequence identified by AF061836 contains 1822 nucleotides. Claim 9 is directed to a nucleic acid "consisting of" the sequence designated as SEQ ID NOS:1 or 3. SEQ ID NO:3 contains 1680 nucleotides. Therefore, claim 9 is not anticipated.

Claim 10 relates to a variant of SEQ ID NOS:1 or 3, presenting with *one* type of modification, *i.e.*, either a nucleotide modification or nucleotide deletion, but not both types of modifications. The AF061836 sequence differs from the claimed variants because it presents with both nucleotide modification and deletions (gaps). Consequently, the variants of claim 10 are not anticipated by the AF061836 sequence.

The sequence designated as AF061836 has only a 98.2 % identity with SEQ ID NO:3. For example, some nucleotides differences can be found at the positions 1040 and around nucleotides 1620 to 1630 as well as some gaps for example in position 1492. Thus, new claim 21, which is directed to a variant having at least 99.999 % homology with SEQ. ID NO:3, is

not anticipated.

Thus, withdrawal of this rejection is respectfully requested.

NEW GROUNDS OF REJECTION

Claims 16, 17, 19 and 20 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. For the following reasons, this rejection is respectfully traversed as it applies to pending claims 16 and 20.

The Examiner states that he cannot find any explicit or implicit teaching of a vector comprising both SEQ ID NO:1 and 3 in the cited teachings or anywhere else in the specification.

Claim 16 as amended is directed to a vector comprising a polynucleotide consisting of SEQ ID NO:1 *or* a polynucleotide comprising SEQ ID NO:3. Thus, such vectors are described in the specification at least in example 9, pages 41-42. Claim 20 is no longer dependent on claim 16. Besides, it does not recite a vector containing both SEQ ID NOS:1 and 3.

Thus, withdrawal of this rejection is respectfully requested.

Claims 2, 6, 9-11 and 16-20 have been rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

As explicitly stated in the Action, the rejection focuses on enablement for screening assays and the agents identified thereby. The Examiner's position is that a disclosure for a method of identifying an agent having a specific activity must not only enable the method but must also teach the skilled artisan how to use the agent identified by the method without undue experimentation. Applicants disagree.

The rejected claims are directed to nucleic acids, variants of the nucleic acids, recombinant vectors and host cells and compositions. The claims certainly embrace genetic reagents or

tools useful in practicing the screening method. On the other hand, Claim 4 is directed specifically to the screening assays; Claim 5 is directed to a modulating compound identified from that assay; and claim 12 is directed to a pharmaceutical composition comprising the modulating compound and a pharmaceutically acceptable carrier. However, claims 4, 5 and 12 have been withdrawn from further consideration as being drawn to non-elected inventions. Thus, none of the rejected claims is actually directed to a screening assay, a modulating agent identified using the method, or a pharmaceutical composition containing a modulating agent identified using the method. Therefore, the scope and enablement of these claims are not presently at issue. Therefore, the issues of whether RasSF1 occurs in all cancers, or cancers other than breast, lung and ovarian cancers, and whether modulation of its interaction with βTrCP would be therapeutic in those cancers, are believed to be irrelevant to the issue of whether the rejected claims are enabled. A patent application is required to enable an invention only with respect to the *claimed subject matter*. See *In re Moore*, 439 F.2d 1232, 169 USPQ 236, 238-239 (C.C.P.A. 1970)(emphasis added). Thus, in accordance with *In re Geerdes*, 35 U.S.C. Section 112, first paragraph, requires only that enablement correspond with the scope of the claimed invention and the Examiner may not demand more from an applicant. 491 F.2d 1260, 180 USPQ 85, 88 (C.C.P.A. 1970). Withdrawal of the rejection on this basis alone is requested.

Aside from the foregoing, the screening methods are clearly enabled. See, *e.g.*, ¶¶89 (or pages 13 *et seq.*) and the prior art referenced therein. These techniques, and particularly the two-hybrid screening, are well known in the art, and sufficient data are given in the specification to establish that protein-protein interactions between βTrCP and RasSF1 do occur.

To the extent that the usefulness or utility of the

disclosed methods are in question, Applicants disclose, for the first time, the specific interaction between βTrCP and RasSF1. Applicants underline the importance of RasSF1 in tumorigenesis in breast, lung, and ovarian cancers, since its inactivation has been associated with the cancer process. Therefore, RasSF1 appears to be a transversal protein involved in different types of cancer. Applicants show that the RasSF1 and βTrCP interact together, and that the modulation of RasSF1 expression has consequences on the level of other proteins, such as β-catenin, which is known to be a partner of βTrCP. The action of RasSF1 on a βTrCP partner indicates that the expression of RasSF1 and that of βTrCP are interconnected. Consequently, Applicants' assertion that the interaction of βTrCP with RasSF1 may influence activity of RasSF1 cannot be said to be a simple speculation, since Applicants report in the present specification many results showing the interconnection of the expressions of RasSF1, of βTrCP and of their corresponding partners.

The present invention relates to a new binding-partner of RasSF1 that is known to be involved in tumor process, and allows the precise mapping of the interaction domains of both proteins. This defines a new approach to modulate the activity of RasSF1, by identifying a new partner that interacts with RasSF1 and can protect it from inactivation. Thus, modulators identified by the methods may prove useful in cancer therapy.

The present specification provides sufficient scientific data on the interaction of βTrCP and RasSF1, and the consequences of this complex on other proteins, such as β-catenin. It is also provides the scientific proof that the interaction is linked to a various cancers, through a pathway. The Applicants submit that the present invention is enabled.

Thus, withdrawal of this rejection is respectfully requested.

Claims 20 has been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite with respect to the recitation "a vector consisting essentially of SEQ ID NO:1."

Claim 20 has been amended. Applicant submits that it would be clear and definite to a person skilled in the art. Withdrawal of the rejection is requested.

From the foregoing, favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

As it is believed that all of the rejections set forth in the Official Action have been fully met, favorable reconsideration and allowance are earnestly solicited.

If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that he/she telephone applicant's attorney at (908) 654-5000 in order to overcome any additional objections which he might have.

If there are any additional charges in connection with this requested amendment, the Examiner is authorized to charge Deposit Account No. 12-1095 therefor.

Dated: January 13, 2005

Respectfully submitted,

By Shawn P. Foley

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